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Opioid-free anesthesia with nociception monitoring in bariatric surgery: Is it effective enough?

Nociception monitoring in opioid-free anesthesia

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Abstract
Aim: In this study, we aimed to compare the effectiveness of an opioid-free anesthesia method with Nociception Level (NOL) Index monitoring to provide intraoperative analgesia control in laparoscopic bariatric surgeries and its effect on the risk of postoperative nausea and vomiting and the need for antiemetics and analgesics with the opioid-based anesthesia.
Material and Methods: Forty patients who underwent laparoscopic bariatric surgery were classified into two groups: those who received opioid-based anesthesia (OA) and those who received opioid-free anesthesia (OFA). Intraoperative NOL index values and additional analgesia requirements were noted. Additional analgesia was administered when the postoperative Visual Analogue Scale (VAS) score was ≥3, an antiemetic drug was administered when the nausea-vomiting score was ≥ 2, and their amounts were noted.
Results: There were no significant differences between the groups in terms of NOL values ($p>0.05$) and maximum-minimum NOL values (69.55 ± 8.52 vs. 74.50 ± 8.46, 0 vs. 0, $p>0.05$). Similarities were found between intraoperative and postoperative additional analgesia, VAS score, nausea-vomiting score, and antiemetic drug consumption ($p>0.05$). Tramadol consumption in the first postoperative 24 hours was significantly higher in the OA group (150.0 ± 48.7 mg vs. 110.0 ± 44.7, $p= 0.012$).
Discussion: Opioid-free anesthesia with intraoperative nociception monitoring can be safely applied in bariatric surgery patients.

Keywords
Obesity, Bariatric Anesthesia, Opioid-Free Anesthesia, Nociception

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Introduction

Obesity is a universal health problem that can cause comorbid conditions. Bariatric surgery is among effective treatment options for constant weight loss [1]. It is known that obesity is a risk factor for opioid-induced respiratory depression, and patients undergoing bariatric surgery are at high risk for thromboembolism. Thus, it is desirable to use anesthetic techniques that support quick discharge, minimal postoperative sedation, and early ambulation [2]. There are also some effects of opioids, such as exacerbation of obstructive sleep apnea syndrome (OSAS), increasing postoperative nausea-vomiting (PONV), sedation, and hyperalgesia, which may accompany obesity. Therefore, the use of opioid-free anesthesia in bariatric surgery has become a popular technique for confronting the risks of opioid-related adverse drug events [3]. In opioid-free anesthesia, which has become increasingly popular among anesthetists, it is intended to provide quality anesthesia using multiple non-narcotic medications (ketamine, lidocaine, magnesium sulfate, dexamethasone, dexmedetomidine, etc.) or techniques together, without giving opioids and protecting the patient from the adverse effects of opioids [4,5].

There are questions about whether opioid-free anesthesia provides intraoperative sufficient nociception control [6]. Nociception is a sensory process that includes the detection of stimuli that may be harmful or potentially harmful, and the formation of a response to these stimuli from the central nervous system. Intraoperative nociception monitoring can help provide hemodynamic control, reduce stress response, and predict postoperative pain intensity. NOL Index is the monitoring method with the largest number of parameters that measure intraoperative nociception level [7]. The NOL index value is between zero (0)-hundred (100). The number zero indicates that there is no nociceptive response, the number of hundred refers to the severe nociceptive response. Keeping the NOL index value below 25 indicates that a physiological response is suppressed to harmful stimuli and sufficient analgesia. Falling below 10 may indicate an excessive anti-nociceptive response and the dose of analgesic drug should be reduced [7,8].

Our study was planned to divide patients with laparoscopic bariatric surgery into 2 groups, who were randomly administered intraoperative opioids and non-opioid anesthesia, and to evaluate the effects of intraoperative NOL index monitoring, and the effects of two anesthesia types on nociception control, PONV, analgesic and antiemetic needs.

Material and Methods

Study Design

After obtaining the approval of the ethics committee (SUKAEK 2020/5/1- 16 June 2020) and informed voluntary consent of patients, the present prospective, observational, single-center study was carried out between June 2020 and December 2020. It was planned as a single-blinded, randomized study. The group randomization of patients was achieved according to the order of their admission to the operating room by the investigator giving anesthesia. Forty-four patients who were scheduled to undergo laparoscopic bariatric surgery under general anesthesia and signed the ASA II-III informed consent form were included in the study. Exclusion criteria were those who refused to participate in the study, those with arrhythmias that could affect the NOL Index measurement, those using beta-blocker drugs, those with peripheral vascular disease, and those with a history of allergy to the drugs in the study. Patients who had intraoperative arrhythmia, pulmonary and surgical complications, whose hemodynamic stabilization could not be easily provided, and whose monitoring was interrupted were excluded from the study.

Protocol

We randomized 44 patients in the study. The number of patients was determined equally for the two groups, Group OA and Group OFA, so that the anesthesia methods would be alternating. Information was recorded on age, sex, body mass index (BMI), smoking and comorbidity. Electrocardiography (ECG), non-invasive blood pressure, pulse-oximetry, bispectral index monitoring with a forehead probe (BIS™ Medtronic, Covidien P/N 185-0151), NOL Index monitoring (PMD-200™, Medasense Biometrics Ltd., Israel) with a non-invasive finger probe were administered to the patients.

The patients' basal measurements were recorded, and then 0.03 mg/kg midazolam (Zolamide 5 mg/5 ml; Defarma, Turkey) was administered IV to both groups as a premedication, and oxygen was provided to the patients with a nasal cannula at 4 l/min.

Dexmedetomidine (Dextomid 200 mcg/2 ml, Polifarma, Turkey) 0.5 mcg/kg/h was administered as an IV infusion to Group OFA for 10 min before induction, and the same dose was maintained in induction. Magnesium sulfate (Magnesium sulfate 1500 mg/10 ml, Galen, Turkey) was administered to 30 mg/kg as an IV infusion in 100 ml of saline for 10 min, and 1.5 mg/kg lidocaine (Lidon, 100 mg/5 ml, Onfarma, Turkey) was administered as an IV bolus. Remifentanil (Rentanil 2 mg, Vem, Turkey) 0.05 mcg/kg/min was started as an IV infusion for group OA, and this dose was administered for 10 min before induction. It was administered as an IV infusion at 0.1 mcg/kg/min during induction. Before induction, the patients in both groups were preoxygenated with 100% oxygen at 6 l/min using an anesthesia face mask.

Both groups received propofol (Propofol 1% 20 ml, Fresenius kabi, Germany) 2 mg/kg IV and rocuronium (Muscobloc 50 mg/5 ml, Polifarma, Turkey) 1 mg/kg IV during induction. Complete relaxation and unresponsiveness were ensured, and then the patients were intubated and connected to the anesthesia device. The ideal weight of the patients was calculated according to the Broca Index and the medication was administered accordingly.

50% oxygen + 50% desflurane was administered in air for maintenance in both groups, and desflurane inhalation was adjusted so that the BIS would be between 40-50. Moreover, it was planned to administer 0.05-0.2 mcg/kg/min IV remifentanil infusion in Group OA and 0.2-0.7 mcg/kg/h IV dexmedetomidine infusion in Group OFA. The range of 10-25 is regarded the ideal value of the NOL Index for sufficient analgesia under anesthesia. Based on this range, dexmedetomidine and remifentanil infusion doses used in maintenance were adjusted. Dexmedetomidine infusion dose and remifentanil infusion dose were reduced by 0.1 mcg/kg/h and 0.05 mcg/kg/min, respectively, when the NOL value was below 10 for more than 120 seconds, and when required, they were reduced to

the lowest level of the infusion dose range determined for both drugs. They were increased to the top of the infusion dose range determined for both drugs when it was above 25 for more than 60 seconds. When the NOL value was still above 25 for more than 120 seconds, although the infusion was administered at the upper level of the mentioned drug doses, the patients were administered 20 mg of tenoxicam (Tilcotil 20 mg/2 ml, Deva, Turkey) IV, and the patients who received additional analgesia were recorded. Intubation, incision, and trocar intervention were determined as the stimuli that might lead to pain, and they were entered into the NOL Index device as data. While the 'period before' the determined painful stimuli was considered as the average of the NOL values of the 30-second time period just before the painful stimulus was given, the 'period after' was considered as the average of the NOL values of the 180-second time period immediately after the painful stimulus was given. Time (T), infusion initial-induction (T1), induction-intubation (T2), pre-intubation (T3), post-intubation (T4), pre-incision (T5), post-incision (T6), pre-trocar (T7), post-trocar (T8), final trocar insertion-extubation (T9), induction-extubation (T10), and infusion initial-extubation (T11) were determined as the time intervals, and the average of the NOL index values in these ranges was taken.

Thirty minutes before the end of the surgery, all patients received 1 g of paracetamol (Parol 10 mg/ml, Atabay, Turkey) as an IV infusion, and 8 mg of ondansetron IV (Kemoset 8 mg/4 ml, Deva, Turkey). Following the removal of trocars, dexmedetomidine, and remifentanil infusions were stopped. Desflurane was ceased when the final surgical suturing was initiated. Sugammadex (Bridion 200 mg/2 ml, Merck Sharp Dohme, USA) was administered intravenously at a dose of 4 mg/kg at the end of surgery to antagonize neuromuscular blockade in patients without intraoperative complications, and the patients were extubated after achieving sufficient spontaneous respiratory effort (vital capacity ≥ 10-15 ml/kg).

The patients' VAS score, nausea/vomiting score, analgesic and antiemetic requirements were recorded at the 5th, 15th, and 30th minutes of their admission to the recovery room after surgery (Nausea and vomiting score: 0- no complaints, 1- mild nausea, 2- moderate nausea, vomiting, 3- frequent vomiting, 4- severe vomiting [9]). During the recovery room follow-ups, patients with nausea and vomiting score ≥ 2 were given IV Metoclopramide (Metpamide 10 mg/2 ml, Sifar, Turkey)10 mg as an antiemetic and 100 mg of tramadol (Tradolex 100 mg/2 ml, Menta, Turkey) IV when their VAS score was ≥3, and this was recorded.

Whenever the VAS score was ≥3, it was planned to administer tenoxicam 20 mg and paracetamol 1 g IV, respectively, to the patients who were followed up postoperatively. The patients who did not respond to these two analgesics during their follow-ups were planned to be administered 50 mg of tramadol IV. Thus, it was intended to compare the two groups in terms of opioid requirements in the postoperative period. The patients' postoperative VAS scores at the 2nd, 6th, 12th and 24th hours and total antiemetic, tenoxicam, paracetamol, and tramadol doses in the first 24 hours were recorded.

Statistical analysis

Since the t-test would be performed for the data to be obtained from this study's results, when the sample size of α=0.01 (error) and a power of the test of 99% were taken into account according to the power and sample size test, in relation to previous studies in this field (Elsaye et al., 2019), it was calculated that it was necessary to conduct research with a minimum of 15 individuals per group. However, taking into account the risk of any problems with patients, it was considered appropriate to conduct research with 22 people per group, namely, 44 people in total in the study. Since 4 patients of 44 patients experienced interruptions in intraoperative follow-up, they were excluded from the study, and the study was completed with 20 patients per group and 40 patients in total. IBM SPSS V23 was used to analyze the data. The Shapiro-Wilk test was performed to test the conformity to the normal distribution. When comparing categorical variables by groups, the Chi-square and Fisher's Exact tests were used. While the independent two-sample t-test was used to compare the normally distributed quantitative data according to the paired groups, the Mann-Whitney U test was used for the comparison of the non-normally distributed data. Whereas the Friedman test was used to compare the quantitative data that were not normally distributed three and more times within the groups, the repeated analysis of variance was used for the comparison of normally distributed data. The analysis results were presented as mean ± s. deviation and median (minimum-maximum) for quantitative data and as frequency (percentage) for categorical data. P<0.05 was considered the level of significance.

Ethical Approval

Ethics Committee approval for the study was obtained.

Results

We randomized forty- four patients in the study, but four patients

Table 1. Patients' Main Characteristics (n= 40).

	Group OA (n=20)	Group OFA (n=20)	p *
Female/Male (Number of Patients)	19/1	18/2	1.000
Age (years)	36.1 ± 11.8	34.3 ± 12.2	0.637
Height (cm)	161.7 ± 6.9	161.2 ± 7.3	0.838
Weight (kg)	125.4 ± 20.5	114.3 ± 16.0	0.099
BMI (kg/m^2)	47.9 ± 7.1	44.0 ± 4.4	0.091
ASA II/III (Number of patients) (%)	10(50)/10(50)	8(40)/12(60)	0.525
Smoking (no/yes) (%)	14(70)/6(30)	17(85)/3(15)	0.451
Type of Surgery (number) (percent)			
Lap. sleeve	11 (55)	11 (55)	1.000
Lap. OAGB	5 (25)	5 (25)	
Lap. gastric bypass	4 (20)	4 (20)	
Comorbidity (%)			
No	14 (70)	12 (60)	0.846
Asthma	3 (15)	2 (10)	
Diabetes (DM)	1 (5)	2 (10)	
Hypertension (HT)	1 (5)	2 (10)	
DM+HT	1 (5)	1 (5)	
Duration of surgery (min)	114.4 ± 30.9	117.6 ± 34.6	0.756
Duration of anesthesia (min)	138.2 ± 34.6	139.3 ± 38.5	0.925

The data were expressed as patient number ratios, mean ± standard deviation, or absolute value (percentage). *p<0.05 was considered statistically significant. n: number of patients, OA: Opioid Anesthesia, OFA: Opioid Free Anesthesia, cm: centimeter, kg: kilogram, m^2: square meter, lap.: laparoscopic, min: minute, OAGB= One Anastomosis Gastric Bypass

Table 2. Intraoperative NOL Values.

	Time	Group OA		Group OFA		Test statistics	p
		Mean ± SD	Median (min. - max.)	Mean ± SD	Median (min. - max.)		
NOL	T1	16.96 ± 9.63	14.35 (3.89 – 43.25)ab	15.36 ± 8.20	13.50 (6.58 – 32.90)abf	U=0.482	0.482
	T2	33.07 ± 9.69	34.20 (17.96 – 53.31)d	29.52 ± 10.33	29.74 (12.71 – 48.00)ec	U=0.279	0.279
	T3	28.10 ± 15.89	29.20 (0.00 – 55.60)ad	26.32 ± 12.49	26.46 (0.00 – 43.00)cdef	U=0.695	0.695
	T4	45.90 ± 11.99	45.23 (26.57 – 68.65)d	40.80 ± 10.28	41.23 (18.30 – 55.81)c	U=0.256	0.256
	T5	4.43 ± 4.48	3.00 (0.00 – 15.00)c	5.03 ± 5.29	3.59 (0.00 – 20.33)b	U=0.807	0.807
	T6	15.46 ± 10.11	12.16 (0.97 – 36.59)abc	20.06 ± 8.67	20.50 (3.08 – 34.70)ade	U=0.094	0.094
	T7	13.41 ± 8.48	12.25 (3.00 – 38.67)abc	11.94 ± 7.59	13.28 (0.30 – 30.33)ab	U=0.705	0.705
	T8	25.98 ± 15.13	23.76 (4.67 – 52.16)bd	16.25 ± 7.47	16.71 (3.70 – 30.22)ade	U=0.074	0.074
	T9	14.52 ± 4.32	14.61 (6.64 – 22.91)ac	12.40 ± 4.48	11.65 (5.08 – 20.90)ab	U=0.137	0.137
	T10	15.58 ± 4.19	16.25 (8.15 – 22.70)ab	13.87 ± 4.09	13.25 (6.47 – 21.18)abd	U=0.204	0.204
	T11	15.52 ± 4.11	15.94 (8.46 – 22.36)ab	13.92 ± 3.90	13.51 (6.82 – 21.40)abd	U=0.224	0.224

NOL: Nociception Level Index, OA: Opioid Anesthesia, OFA: Opioid Free Anesthesia, T: Time, U: Mann-Whitney U test statistics, : Friedman test statistics, t: Independent two-sample t-test statistics, F: Repeated analysis of variance, a-f: No difference between the times with the same letter within the groups, mean ± s. deviation, median (minimum-maximum)

Table 3. Recovery and Postoperative First 24-Hour VAS Scores.

	Time	Group OA	Group OFA	Test Statistics	p
Recovery Room VAS	Arrival	5.5 ± 1.7 6.0 (2.0 – 8.0)	4.6 ± 1.8 5.0 (1.0 – 7.0)	t:1.554	0.138
	5th min	4.7 ± 2.0 5.0 (1.0 – 7.0)	3.8 ± 1.8 4.0 (1.0 – 7.0)	t:1.444	0.184
	15th min	3.6 ± 1.5 4.0 (0.0 – 5.0)	3.0 ± 1.5 3.0 (0.0 – 5.0)	t:1.262	0.208
	30th min	2.4 ± 0.9 3.0 (0.0 – 3.0)	2.1 ± 1.1 2.0 (0.0 – 3.0)	t:1.11	0.416
Postoperative VAS	2nd h	4.7 ± 1.9 4.5 (2.0 – 8.0)	4.0 ± 2.3 4.0 (0.0 – 7.0)	U=167.5	0.373
	6th h	3.0 ± 1.6 3.0 (0.0 – 6.0)	2.8 ± 1.5 3.0 (0.0 – 5.0)	U=195.0	0.889
	12th h	2.6 ± 1.5 2.0 (0.0 – 6.0)	2.6 ± 1.9 2.0 (0.0 – 6.0)	U=188.0	0.740
	24th h	1.1 ± 0.8 1.0 (0.0 – 2.0)	1.1 ± 0.6 1.0 (0.0 – 2.0)	U=199.0	0.976

OFA: Opioid Free Anesthesia, OA: Opioid Anesthesia, VAS: Visual Analogue Scale, mean ± standard deviation, median (minimum-maximum), p≤0.05 was considered significant. t: Independent two-sample t-test statistics, U: Mann-Whitney U test statistics

were excluded from the study because of the interruption in the follow-up of intraoperative NOL monitoring. Therefore, the study was conducted with 40 patients.

Table 1 shows the patients' demographic characteristics. No significant difference was found between the two groups in terms of demographic data, type of surgery, duration of surgery, and duration of anesthesia (p> 0.05).

Intraoperative Evaluation

The value of the intraoperative target NOL Index was taken as the range of 10-25 under general anesthesia. In OA and OFA groups, induction-intubation (T2), pre-intubation (T3) and postintubation (T4) time periods, NOL Index value averages were above 25. The mean value of NOL was found to be 25.98 ± 15.13 in the post-trocar (T8) time period in the OA group and was above 25, but there was no statistical difference between the two groups (Table 2). In the intraoperative period, it was observed that the mean NOL Index values were below 25 in both groups in other time periods (Table 2).

In the specified time periods, there was no significant difference between the groups in terms of NOL values (p>0.05) (Table 2). In both groups, while the highest median NOL value was obtained after intubation (T4), the lowest median NOL value was obtained before incision (T5). The highest median NOL values were 45.23 and 41.23 in the OA and OFA groups, respectively. The lowest median values were found to be 3 and 3.59 in groups OA and OFA, respectively. No statistically significant differences were found between the two groups (p>0.05).

No differences were found between the groups in terms of the distributions of the maximum and minimum NOL values (69.55 ± 8.52 vs. 74.50 ± 8.46, 0 vs. 0, p>0.05). Four individuals needed additional intraoperative analgesia in the OA group and one individual in the OFA group, but there was no statistical difference between them (p= 0.342).

Postoperative Evaluation

In postoperative follow-ups in the recovery room, no statistical differences were found between the two groups in the nausea-vomiting scores (0.7 ± 0.7 vs. 0.4 ± 0.7) (p> 0,05). In the follow-ups in the postoperative recovery room, one person in each group did not need analgesics. While 3 people in the OA group needed antiemetics, 2 people in the OFA group needed antiemetics. However, there was no statistically significant difference between the two groups in terms of analgesic and antiemetic requirements (p>0.05). There were also no statistical differences between the two groups in the postoperative recovery room and VAS score follow-ups in the first 24 hours (Table 3) (p> 0.05).

While no differences were found between the number of tenoxicam (37.0 ± 7.3 mg vs. 32.0 ± 12.0 mg), paracetamol (1526.3 ± 611.8 mg vs. 1500.0 ± 760.9 mg) and the number of antiemetic use (1.0 ± 0.9 vs. 1.0 ± 0.7) in the postoperative first 24 hours, the tramadol (opioid) requirement was statistically significantly higher in the OA group compared to the OFA group (150.0 ± 48.7 mg vs. 110.0 ± 44.7 mg, p<0.05).

Discussion

In our study, the intraoperative nociception level was monitored by the NOL index in bariatric surgery patients, and analgesic drug administration was performed according to the NOL Index

value. In our study, we observed intraoperative nociception control was similar in group OA and group OFA. Initial trials used hemodynamic parameters to guide the intraoperative administration of analgesics, but it was impossible to achieve standardization, and no clear evaluation could be obtained [10]. There are studies on the use of opioid-free anesthesia in bariatric surgery, but no objective evaluation method has been used in any of them. Hemodynamic parameters can be misleading in determining nociception control and analgesic need. Most anesthetic and analgesic drugs may conceal the hemodynamic responses to pain, such as increased heart rate and blood pressure, by causing bradycardia and vasodilation [11, 12, 13]. The NOL index is a unique multiparameter-based nociception measurement method. [7]. The NOL Index was preferred in our study to achieve an objective measurement.

In the study by Schwab et al., patients who were intended to undergo gynecological-urological surgery were divided into groups with fentanyl use and multimodal (lidocaine, magnesium, ketamine) low-dose opioid analgesia and were followed up with the NOL device. NOL was observed to be similar between the two groups, and no evidence was found regarding that the low-dose opioid technique was associated with more intraoperative or postoperative pain [14]. Gazi et al. followed the patient groups who received intraoperative remifentanil and dexmedetomidine with ANI in hysteroscopy cases, and ANI, another nociception monitor, could be kept within the targeted limits in both groups [15]. In our study, OA and OFA groups were followed with an intraoperative NOL Index device. Within the specified time periods, the intraoperative NOL index values were similar between the two groups. There was no difference between the highest and lowest NOL Index values obtained in both groups in the intraoperative period, and postoperative VAS values were similar.

In the study by Jildenstal et al., painful stimuli were accepted such as chin lift, intubation, bladder catheterization and incision, and NOL values increased in all patients after chin lift and intubation. [16]. In the study by Stöckle et al., based on the NOL Index at different doses of remifentanil, the highest NOL Index value was observed after intubation [17]. These studies argued that the NOL Index showed nociceptive responses earlier and more frequently than hemodynamic parameters and was a reliable marker for optimal analgesic administration. In the current study, the fact that the average of the NOL Index was above 25 before intubation originated from the chin lift maneuver and the highest NOL Index value was obtained after intubation in both groups. The average NOL Index after the trocar settlement was found to be over 25 in the OA group, but no statistical differences were found between the two groups. In our study, similar to other studies, the response to the painful stimulus was determined with the NOL Index.

In the study, conducted by Jebaraj et al., on 30 robotic urological surgery patients, the groups receiving propofol-fentanyl and propofol-dexmedetomidine in the intraoperative period were compared, analgesia follow-up was performed according to hemodynamic parameters in the intraoperative period, and an additional dose of fentanyl was administered in cases of hypertension/tachycardia. In the dexmedetomidine group, rescue analgesia was less needed. It was concluded that dexmedetomidine could provide as much analgesia as fentanyl in the intraoperative period and could be used as a stand-alone analgesic agent [18]. Another study argued that dexmedetomidine alone could not provide sufficient intraoperative analgesia and there would be an additional analgesia requirement [19]. Jin et al. suggested that the need for additional analgesia was less than with the use of intraoperative dexmedetomidine compared to remifentanil [20]. In our study, magnesium and lidocaine were applied to patients in the OFA group before induction and dexmedetomidine infusion was performed in the intraoperative period. Remifentanil was administered to the OA group. Four patients in the OA group and 1 patient in the OFA group needed additional analgesia, but no statistically significant differences were found between them.

In the study by Bakan et al. in laparoscopic cholecystectomy cases, patients administered with intraoperative dexmedetomidine-lidocaine (opioid-free anesthesia) were compared with patient groups administered with remifentanil (opioid-based anesthesia), and it was revealed that opioid consumption, maximum pain score, and additional analgesia requirement in the 2nd postoperative hour were significantly lower in the opioid-free anesthesia group [21]. In the study by Salman et al. on laparoscopic gynecological surgery patients with ANI it was observed that postoperative pain scores and additional analgesia requirements were similar between the two groups followed up with intraoperative dexmedetomidine and remifentanil infusions, nausea and vomiting were more common in the group taking opioids [22].

The present study found that postoperative tramadol consumption was significantly higher in the group using intraoperative opioids. The postoperative early VAS score and nausea-vomiting score were lower in the OFA group, but no statistical differences were found, and 24-hour VAS follow-ups were revealed to be similar in both groups. While opioids may lead to hyperalgesia when used with intraoperative infusion, the analgesic effect is observed when they are applied in the postoperative period. Dexmedetomidine does not have this effect, and there are even publications indicating that it has a synergistic effect with opioids and prevents hyperalgesia by modulating the expression of NMDA receptors. Dexmedetomidine exerts an analgesic effect through alpha 2 adrenergic receptors in the spinal cord and maintains normal nociceptive responses [20,23].

Mulier et al. compared the groups of patients who received intraoperative sufentanil and dexmedetomidine with lidocaine in patients with laparoscopic bariatric surgery. In the intraoperative period, 2 g of paracetamol IV infusion for postoperative pain control, 1 g of paracetamol IV every 6 hours postoperatively, and patient-controlled analgesia and morphine boluses without continuous infusion were planned for both groups. In the early postoperative evaluation of patients, the mean VAS score (4.9 vs. 1.7), opioid consumption (15.3 mg morphine vs 4.9 mg morphine), and the frequency of nausea and vomiting were found to be higher in the opioid group [24]. We administered 1 g of paracetamol IV infusion intraoperatively to our patients for postoperative analgesia. In our study, there was a period when the VAS score was ≥3 in the first 30 minutes postoperatively, except for one person in both

patient groups, additional analgesia was required, and tramadol was administered. The dose of paracetamol administered intraoperatively can be increased or another analgesic drug can be administered in addition to paracetamol to improve early postoperative pain outcomes.

In obesity surgery, there is a transition to opioid-free anesthesia, due to the side effects of opioids, but in the literature, there is no study objectively comparing the intraoperative nociception control of opioid-free anesthesia with opioid anesthesia. Our study has shown that similar nociceptive control is provided between NOL Index monitor and two types of anesthesia and shed light on suspicions.

Our study has some limitations. The first is that it is single-centered and only in patients with laparoscopic bariatric surgery. Secondly, in the literature, opioid-free anesthesia is available in different definitions and applications with different drug combinations. In our study, magnesium, lidocaine, and dexmedetomidine were preferred in the group of opioid-free anesthesia. Different drug combinations can be performed in patients with bariatric surgery. Thirdly, in the intraoperative period, especially before and after painful stimuli, heart rate and blood pressure could be monitored and compared to NOL index values.

Conclusion

It was seen that similar intraoperative and postoperative analgesia control was provided by opioid-based and opioid-free anesthesia methods in patients bariatric surgery. Intraoperative nociception monitoring with the NOL Index allowed to objectively monitor the effective control of intraoperative analgesia in bariatric surgery patients in both anesthesia methods. The group with opioid-based anesthesia needed more postoperative opioids. We think that opioid-free anesthesia can be preferred in bariatric surgery patients to avoid the adverse effects of opioids. Opioid-free anesthesia can be evaluated with intraoperative pain monitoring by conducting similar studies with other opioid-free anesthesia protocols.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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